Remarks

Applicant notes with appreciation the detail and thoroughness of the Office Action dated June 9, 2008 (hereinafter "the Office Action"). Applicant respectfully requests reconsideration of the above-identified application in view of the following remarks.

Currently, claims 1-21 are subject to examination on the merits.

At the time of the Office Action, the specification was suggested to be revised according to 37 C.F.R. 1.77(b). Claims 6 and 14 were objected to for improper use of abbreviations. Claims 1-21 were rejected under 35 U.S.C. 112, 2nd paragraph. Claims 1-21 were rejected under 35 U.S.C. 112, 1st paragraph for lack of enablement. Claims 1-3, 14-16, and 20-21 were rejected under 35 U.S.C. 102(b) over Dincturk et al. (J. BIOSCI., 2001, 26(5), 635-40; hereinafter "*Dincturk*").

By this amendment, claims 1-2, 6 and 14 have been amended in traversing the above-identified claim objections and rejections. Support for the amendment is found, *inter alia*, at lines 3-4 on page 1, lines 18-19 on page 12, and line 13 on page 11 to line 2 on page 12 of the Specification originally filed, and in the claims originally filed. No new matter is introduced by this amendment.

Remarks Directed To The Claim Objections

Claims 6 and 14 are objected to for reciting the acronym "EDTA" and the acronym "Con A", respectively, without presenting a full term thereto (¶ 5 of the Office Action).

Responsive to the instant objection, claims 6 and 14 have been amended to recite "ethylene-diamine-tetra-acetic acid (EDTA)" and "Concanavalin A (Con A)", respectively. Support for the Amendment is found at lines 3-4 on page 1 and lines 18-19 on page 12 of the published specification. No new matter is introduced by this Amendment.

Reconsideration and withdrawal of the instant objections to claims 6 and 14 is requested.

Remarks Directed To Claim Rejection Under 35 U.S.C. § 112, 2nd Paragraph

Claims 1-21 are rejected under 35 U.S.C. § 112, second paragraph, as being incomplete "for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: a) expressing a recombinant glucose binding protein in a non-plant host cell, b) producing a lysate containing said glucose binding protein wherein said lysate has a reduced glycogen content and c) recovering said glucose binding protein." (Paragraph 7 of the Office Action.) For at least the reasons stated below, Applicant respectfully traverses the rejections in light of the instant claim amendment.

MPEP 2172 in relevant portions provides:

> **2172 Subject Matter Which Applicants Regard as Their Invention**
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> **1. FOCUS FOR EXAMINATION**
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> A rejection based on the failure to satisfy this requirement is appropriate only where applicant has stated, somewhere other than in the application as filed, that the invention is something different from what is defined by the claims. In other words, ***the invention set forth in the claims must be presumed, in the absence of evidence to the contrary, to be that which applicants regard as their invention.*** *In re Moore*, 439 F.2d 1232, USPQ 236 (CCPA 1971).
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> **II. EVIDENCE TO THE CONTRARY**
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> Evidence shows that a claim does not correspond in scope with that which applicant regards as applicant's invention may be found, for example, in contentions or admissions contained in briefs or remarks filed by applicant, *Solomon v. Kimberly-Clark Corp.*, 216 F.3d 1372, 55 USPQ2d 1279 (Fed. Cir.. 2000); *In re Prater*, 415 F.2d 1393, 162 USPQ 541 (CCPA 1969), or in affidavits filed under 37 CFR 1.132, *In re Cormany*, 476 F.2d

> 998, 177 USPQ 450 (CCPA 1973). ***The content of applicant's specification is not used as evidence that the scope of the claims is inconsistent with the subject matter which applicants regard as their invention***. As noted in *In re Ehrreich*, 590 F.2d 902, 200 USPQ 504 (CCPA 1979), agreement, or lack thereof, between the claims and the specification is properly considered only with respect . . .
>
> (Emphasis added.)

Here, the subject matter recited in the originally filed claim 1 should be presumed to be that Applicant regards as his invention, absent any contentions or admissions contained in materials other than the specification submitted by Applicant, per the relevant MPEP provisions cited above. In fact, the subject matter of claim 1 being Applicant's invention square finds support in, and is consistent with, Applicant's published specification. By way of example, Applicant regards the key to solving difficulties in isolating recombinant Con A existing in the prior art is "a need for solution formulations and a washing regime that successfully accomplishes the removal of interfering molecules with minimal losses of desired protein product" (p. 10, ll. 5-7).

However, in order to facilitate the prosecution to proceed forward, claim 1 has been amended to recite a method comprising the steps of:

a) expressing said recombinant Concanavalin A in a bacterial host cell;

b) producing a lysate containing said Concanavalin A, wherein said lysate has a reduced glycogen content; and

c) recovering said Concanavalin A.

Claims 2-13 are deemed indefinite because "it is unclear in claim 2 what the treating step does or accomplishes. It is noted that this 'treatment' step does not produce any sort of result." (Office Action dated June 9, 2008, ¶ 8).

In response, claim 2 has been amended to depend from claim 1 and further comprising the step of "adding a buffer, in which glycogen is soluble, but in which said Concanavalin A is insoluble, to the lysate."

Claim 2 as amended is now believed to be in allowable form. Reconsideration and withdrawal of the instant rejections to claim 2 and claims 3-12 dependent therefrom is solicited.

Claim 14 is rejected under this subsection for lack of sufficient antecedent basis. Applicants respectfully traverse this rejection. Claim 14 depends from claim 1 and further includes an additional step of "removing ***any*** Concanavalin A complex formed" (emphasis added). Claim 14 recites an additional step optionally employed at a stage wherein glycogen has not yet been sufficiently removed after the method according to claim 1 has been carried out. Please see the Specification as line 13 on page 11 to line 2 on page 12. It so follows that at a point where a recombinant Concanavalin A has been obtained by the method of claim 1, the recombinant Concanavalin A has been refolded to an active form, so that any residual glycogen forms glycogen-Con A complexes, which can be allowed to precipitate out. Simply put, if the glycogen content has already been sufficiently reduced according to the method of claim 1 such that Con A can be recovered, the additional step recited in claim 14 may not be needed. As such, the term "any Concanavalin A complex formed" is not a necessary composition resultant from the method of claim 1; however, in the event that "any Concanavalin A complex" does form, a method of claim 14 may be employed to facilitate the recovery of Con A protein.

Collectively, rejections to claims 1-21 under 35 U.S.C. 112, 2nd paragraph, are submitted to have been traversed. Reconsideration and withdrawal of the rejections is solicited.

Remarks Directed to Claim Rejection Under
35 U.S.C. § 112, 1st Paragraph

Claims 1-21 are rejected under 35 U.S.C. § 112, first paragraph, because the specification "is not enabling for a method of obtaining all recombinant glucose binding proteins

expressed in non-plant host cells simply by reducing the glycogen content of the cell lysate" (Office Action of June 9, 2008, ¶ 11). To support the above-identified contention, Examiner essentially asserts:

> . . . it is noted that not all glucose binding proteins expressed in non-plant host cells are insoluble simply by expressing them in non-plant host cells. And not all glucose binding proteins will be insoluble in a buffer yet have glucose and other impurities soluble at the same time as this will depend on the glucose binding protein's isoelectric point . . . However, the unique problem of concanavalin A precipitating due to the binding of glycogen does not necessarily extend to all other glucose binding proteins and thus reducing the glycogen content of the host cell or of a lysate may have no effect at all on obtaining said protein. *Id.*

MPEP in relevant portions provides:

> **UNDUE EXPERIMENTATION**
>
> ***The fact that experimentation may be complex does not necessarily make it undue***, if the art typically engages in such experimentation
>
> * * *
>
> In *Wands*, the court noted that there was no disagreement as to the facts, but merely disagreement as to the interpretation of the data and the conclusion to be made from the facts. *In re Wands*, 858 F.2d at 736-40, 8 USPQ2d at 1403-07. The Court held that the specification was enabling with respect to the claims at issue and found that 'there was considerable direction and guidance' in the specification there was "a high level of skill in the art at the time the application was filed;' and '***all of the methods needed to practice the invention were well known***,' 858 F.2d at 740, 8 USPQ2d at 1406. After considering all the factors related to the enablement issue, the court concluded that 'it would not require undue experimentation to obtain antibodies needed to practice the claimed invention.' *Id.* 8 USPQ2d at 1406.

(MPEP 2164.01(a); emphasis added).

As cited above, the Office Action in relevant portion states that "all of the working examples in the specification are drawn to concanvalin A . . . the predictability of whether or not

this particular methodology would work for all other glucose binding proteins is low and a skilled artisan would necessarily have to endure needless experimentation."

Contrary to the Examiner's contention as cited above, the guidance and consideration provided in the instant specification would suffice to enable embodiments of the present invention as recited in claims 1-21, for at least the following reasons.

As detailed on page 1, lines 9-17 of the instant specification, "Con A is a member of a large ***family*** of ***homologous*** carbohydrate-recognizing proteins . . . the saccharide specificity of Con A is ***similar*** to that of the closely related lectins from pea, lentil and broad bean." Having such well conserved homologous structures, it is fair to say Con A, along with its homologous glucose-recognizing family members, would behave similarly in a given condition, such as subject to a buffer.

Moreover, and as indicated above, isolation method used for recombinant pea lectin has also been applied in the art to isolate the related protein, Con A. (Page 6, ll. 18-19.)

Based on the above-identified similarities in the structure and usage between the Con A protein and its related homologous glucose-binding family members, guidance and consideration provided based on the Con A should be fairly and reasonably applicable to the other members of the glucose-binding protein family.

In fact, as with the case of the Con A protein, steps for practicing the present invention with regard to several other Con A homologs have been described in sufficient details.

In optimizing the experimental condition suitable for every member of the glucose-binding protein family may be repetitive, tedious, or even complex, due to factors that each member may have a distinctive isoelectric point as pointed by the Examiner on page 7 of the Office Action. That alone, however, does not equate to "undue" within the context of "undue experimentation" pursuant to MPEP 2164.01 cited above.

It should also be noted that "the prior art does not detail or suggest that the problem of glucose binding proteins precipitating upon bonding glycogen is a problem," as asserted on page 7 of the Office Action, is not only irrelevant to the instant enablement rejection, but also rather speaks to the benefit of the present invention in that the present discovery of glycogen forming complex upon the Con A as neither anticipated nor obvious over the art.

However, in order to facilitate the prosecution to proceed forward, claim 1 has been amended to recite a method comprising the steps of:

a) expressing said recombinant Concanavalin A in a bacterial host cell;

b) producing a lysate containing said Concanavalin A, wherein said lysate has a reduced glycogen content; and

c) recovering said Concanavalin A.

By adopting the changes, as recommended in the relevant portions of the Office Action, into the independent claim 1 and specifically stating the step of expressing said recombinant Con A in a "bacterial host cell", Applicants believe that the independent claim 1 and all the claims dependent therefrom are patentable. Reconsideration and withdrawal of the instant rejections to claims 1-21 under 35 U.S.C. § 112, 1st paragraph, is solicited.

Remarks Directed to Claim Rejections Under 35 U.S.C. § 102

Claims 1-3, 14-16, and 20-21 are rejected under 35 U.S.C. § 102(b) as being anticipated by *Dincturk*.

As stated in paragraph 13 of the Office Action:

> CoA forms a complex with glycogen, and thus when *Dincturk* teaches removing the precipitated Con A by centrifuging the cell lysate, inherently the glycogen-Con A complex is thus removed as well. Therefore, the glycogen content of the cell lysate is also being reduced at the same time.

For at least the reasons stated below, Applicant respectfully traverses the instant rejections.

At a time just prior to the present invention, it was well known in the art that the natural plant source is rich in Con A (p. 1, ll. 19-20). However, Con A from those natural plant source are often subjected to post-translational modifications.

The art had since been well informed of the various forms of recombinant Con A originating from developing seeds and *E. Coli* (p. 4, l. 20 to p. 5, l. 1). Likewise, the art had also been well informed of the use of dextran affinity chromatography for isolating the Con A proteins from the E-Coli cell lysate (p. 5, l. 5 to p. 6, l. 2). However, the affinity chromatography method had been met with limitations due to insufficient yield and lack of appreciable reproducibility (p. 6, ll. 2-17). Other efforts in enhancing expression levels of recombinant CoA did not overcome the above-cited difficulties in purification.

The present invention recognizes that glycogen complexes with Con A and the resultant complex affects the quantity and quality of the recombinant Con A isolated. What is recognized by the embodiments of the present invention is a need for solution formulations and a washing regime that "successfully accomplishes the removal of interfering molecules with minimal losses of desired protein product" (p. 10, ll. 5-7).

According to at least one aspect of the present invention, and as recited in independent claim 1 in current form, a method is provided for isolating Con A comprising expressing said recombinant ***Concanavalin A*** in a bacterial host cell; producing a lysate containing said Concanavalin A, wherein said lysate has a reduced glycogen content; and ***recovering said Concanavalin A***" (emphasis added).

The present invention is concerned with obtaining active ConA. Active ConA does bind glycogen. Thus, the ConA which precipitates is complexed with glycogen. The problem solved by the present invention is how to obtain active ConA, from which interfering substances such as glycogen have been removed. The solution to this problem is to reduce the glycogen content of the lysate. One embodiment of this solution is claimed in claim 2. Here, a buffer is added to the lysate. In this buffer, the ConA is insoluble, but the glycogen is soluble.

Thus, the glycogen bound to the ConA is solubalised, whilst the ConA is not. In this way, the glycogen is removed from the ConA complex.

In direct contrast, *Dincturk* fails to teach or suggest the step of "expressing said recombinant Concanavalin A in a bacterial host cell" as recited in claim 1. At most, *Dincturk* concerns pre-pro-Con A, a precursor form of Con A. As well acknowledged in the art, the pre-pro-Con A of *Dincturk* is different from the mature protein Con A in various aspects including respective DNA and amino acid sequences. Please see lines 20-24 of page 4 and lines 13-17 of page 2 of the instant specification as originally filed. One of the differences is that pre-pro-ConA, being in a precursor form, is inactive and therefore does not bind glycogen. Thus, the precipitation of the pre-pro-ConA is not reducing the glycogen content of the lysate. In addition, the precipitated pre-pro-ConA is not complexed with glycogen.

Thus, Dincturk does not teach a method of obtaining active recombinant ConA. Neither does it teach lysate with a reduced glycogen content. The teaching of Dincturk isn't even relevant to the present invention, as the precipitation of pre-pro-ConA does not encounter the same problems as the precipitation of active ConA (namely, complexing with glycogen).

In addition, *Dincturk* fails to teach or suggest the step of "producing a lysate ... wherein the lysate has a reduced glycogen content." *Dincturk* as a whole teaches the generation of a particular recombinant pre-pro-Con A product that is low in solubility (Title and page 638). It is further contemplated that the low solubility of pre-pro-Con A is due to the presence of a plant signal peptide (page 638). In fact, *Dincturk* entirely fails to mention the word "glycogen", let alone producing a lysate with reduced glycogen content as recited in the independent claim 1.

The very discovery leading to the present invention, namely the discovery of reducing glycogen content and recovering Con A using a buffer which differentiates the Con A from its surrounding impurities such as glycogen, may not be applied to supplement the deficiencies of *Dincturk* in order to render the present claims anticipated or obvious. Moreover, and contrary to what is stated in paragraph 13 of the Office Action, *Dincturk* does not teach or

suggest the step of recovering Con A as recited in claim 1. Rather, as squarely acknowledged by the Examiner, Con A is removed ***together*** with glycogen if ever present, in the form of glycogen-Con A complex.

Since *Dincturk* fails to teach or suggest at least one element of independent claim 1, claim 1 and all the claims dependent therefrom are submitted to be patentable.

Conclusion

Applicant submits that the claims are in condition for allowance and respectfully request a notice to that effect. If the examiner believes that a telephone conference will advance the prosecution of this application, such a conference is invited at the convenience of the Examiner.

The Petition fee of $130.00 is being charged to Deposit Account No. 02-3978 via electronic authorization submitted concurrently herewith. The Commissioner is hereby authorized to charge any additional fees or credit any overpayments as a result of the filing of this paper to Deposit Account No. 02-3978.

Respectfully submitted,

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